With Authors Compliments

ROYAL COLLEGE OF SURGEONS OF ENGLAND

ON

STRYCHNIA HYPODERMICALLY ADMINISTERED

IN

PARALYTIC AFFECTIONS.

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It is proposed in this communication, by the author, to point out the advantages and disadvantages of administering strychnia by the cellular tissue; and to indicate, as far as his practical experience of the use of that alkaloïd has gone, what difference of action may be expected when it is subcutaneously given, from its usual effects when given by the mouth.

Pereira tells us that, "of all diseases for which nux vomica has been employed, in none has it been so successful as in paralysis, and it is deserving of notice that this is one of the few remedies whose discovery is not the result of mere chance, since Fouquier was led to its use by legitimate induction from observations of its physiological effects."[1]

Valuable as strychnia has proved as a nervine tonic, and more particularly in paralysis, there are some forms of nervous debility in which it is not only useless, but even injurious.

Very often strychnia has been given for a considerable length of time in chronic paralytic affections with entirely negative results. The question may be asked why the strychnia has been thus inefficacious, and whether the inertness has been due to its administration by the mouth, or whether the lesion has been of some part of the cerebro-spinal system over which strychnia has no specific action?

Now I think I shall be able to prove that the mode by which this alkaloïd is introduced into the system is one cause of difference of action. That such is the case with morphia and atropia, when introduced by different means into the system, I have long maintained, and am happy to see my views so thoroughly corroborated with regard to those particular alkaloïds by the Hypodermic Committee of the Medical and Chirurgical Society, who have lately concluded their investigations.[1]

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[1] Pereira, 'Materia Medica,' vol. ii, p. 616.

And if morphine can be proved, when introduced into the cellular tissue, to have greater rapidity of action, intensity of effect, economy as to the amount required, certainty of action, and that certain unpleasant symptoms can be avoided by giving it by this means rather than by the mouth, and if the same holds good with respect to some other alkaloïds, as I have shown that it does, it is not unreasonable to anticipate certain advantages from the administration of strychnia also by the cellular tissue.

It is somewhat curious but there seems to me to be a great prejudice on the part of many medical men against—or fear of, the employment of strychnia subcutaneously, even with many who are constantly injecting morphia, a drug which requires quite as much care in its administration.

Certainly one has to study the dose which the constitution of the patient requires more carefully with strychnia than some other alkaloïds, and to begin with a minimum rather than a maximum dose, for the effects from a large dose may be almost too rapidly generated to be subsequently beneficial. Some patients, moreover, are far more susceptible of strychnia thus administered than others, but such is also the case with morphia and opium. In one patient, a lady who was suffering from injury to the spine and severe nervous prostration, after a fall more than a year previously, I found the $\frac{1}{90}$th of a grain of strychnia as large a dose as she could bear; on the other hand most patients bear well the $\frac{1}{30}$th of a grain, and some even the $\frac{1}{24}$th.

That this *mode* of administering strychnia is more powerful than others is shown by the experiments of the Hypodermic Committee upon rabbits, for they found that the $\frac{1}{16}$th of a grain of strychnine was the smallest dose that killed by the mouth, the $\frac{1}{25}$th of a grain by the rectum, and the $\frac{1}{120}$th of a grain "by the skin" as they call it, but more correctly by the *sub*cutaneous cellular tissue. That committee give no experiments or observations of the therapeutic effects in man, but allude to the experience of Dr. Biegel, "who found one case yield to this method," and to my own observations in favour of its usefulness in certain cases.

I will now shortly detail a few cases of paralysis in which I have injected strychnine with benefit; at the same time I would remark that one must not look for the astonishing or suddenly beneficial results which seem to and do at times attend the injection of anodynes in cases of *pain*, of delirium, &c.

Strychnine should be employed as a nerve tonic or nerve-excitant in cases in which active irritation is supposed no longer to be going on about the clot or presumed cause of the lesion.

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[1] We hope shortly to give our readers some account of these investigations.—Ed. *to* 'Brit. and For. Med.-Chir. Rev.'

What we may fairly hope to expect when we inject strychnine is to find a *beneficial* result produced in a *shorter time* and from much *smaller doses* than when it is given by the mouth, and benefit may be expected even in cases which have, as in case 1, been frequently treated, for weeks together, by its stomachic administration without benefit.

Case 1.—Hemiplegia of six years' standing. John C—, æt. 52 years. Had always enjoyed good health, and followed his occupation in the brewery until six years ago, when, whilst at work, he was suddenly seized with loss of power on the left side of the body. He has never since sufficiently recovered to permit of his returning to his occupation, and the utmost he can do is slowly, by the aid of two sticks, to walk about dragging after him the paralysed limb. In addition to the want of power, he nearly always has *pain*, chiefly in the loins after walking a few yards, numbness and coldness, and a sense of weight in the limb, and fatigue from very trivial efforts, so that when out he has been accustomed to stand still frequently to rest, and to walk much bent forwards, chiefly to avoid pain in the loins.

This man had been a patient of mine at the Royal Pimlico Dispensary on and off for several years with these symptoms and loss of power over the bladder, and generally after a few months of stomachic administration of strychnia and other tonics, the symptoms have been moderated for a time. On the 24th of July, 1866, I put him on the $\frac{1}{20}$th of a grain of strychnia—the acetate—with sulphate of magnesia, and some carminatives. This he continued for five weeks twice a day without improvement, except as regards the loss of power over the bladder.

On the 31st of August I began the subcutaneous administration of the alkaloïd, expecting little or no more effect, as so little amelioration had attended the stomachic doses during three or four years.

To sum up briefly, this man, from August 31st to December 1st, that is during three months, had twenty-two strychnine injections; seventeen of these were in quantity the $\frac{1}{30}$th of a grain, the remainder were as strong as the $\frac{1}{24}$th of a grain. During the five weeks which preceded the hypodermic treatment, he had taken as much as *three grains* of strychnia by the mouth without any apparent or palpable effects of the drug upon the paralysed limbs; *but direct strychnine* effects manifested themselves with the *first* as well as with *every* succeeding puncture.

Ten injections were given during the first three weeks. The results were:—1. Rapid improvement in walking power, and increased steadiness of gait. 2. The previous sensation of cold was replaced by a sense of warmth of both legs, chiefly of the paralysed one. This *induced* warmth has never quite subsided, and was always well marked for some hours after the puncture, in fact he almost *complained of* the heat the injections produced throughout his system. 3. The "heavy-weight" sensation in the leg was replaced by a sense of lightness of the limb. 4. The pain both of the loins and leg were removed.

These good results have continued, and he can now walk several miles, more upright, with comparative ease, with little or no pain, and by the aid, for a time, of only one stick.

The question might be put whether the three grains of strychnia previously given by the mouth did not materially assist in these results, seeing that by the cellular tissue he only had altogether about two thirds of a grain?

My reply is simply that he had more than once taken strychnia for two or three months by the mouth without such good results. 2ndly. That the effects from the injection were direct and comparatively immediate. 3rdly. They were such as have been described spontaneously by other patients.

Case 2.—William J—, æt. 60, of Belgrave Buildings. A tall, thin, active, intelligent engine-driver was seized in September, 1863, with right hemiplegia. He was at engine-work when the fit came on. He became insensible, and had much fever, he says, for some days. He gradually improved so as to be able to get about with a stick, but the leg has very little power, feels heavy, and drags; he feels that there is no dependence upon it. The arm is weak, especially the muscles of the upper arm and shoulder, but he can grasp with his fingers.

December 9th.—Omitted medicines by the mouth. I injected the $\frac{1}{90}$th of a grain of strychnia into the arm.

10th.—He felt momentary pains in the course of the evening about the muscles of the forearm and heel; no muscular twitchings, but less "stretchings" of the muscles. Repeated the injection.

11th.—Felt a lightness and freedom in the muscles of the limb. Repeated injection of $\frac{1}{90}$th of a grain.

12th.—Had a few slight muscular twitches in the lumbo-dorsal region on both sides of body. Injected the $\frac{1}{60}$th of a grain.

13th.—The paralysed limbs feel stronger and lighter; has had a few twitches in the right side of the face, right arm, and both legs.

21st.—Has had three more punctures from $\frac{1}{75}$th to $\frac{1}{60}$th of a grain. He had two or three punctures after this date, and by the end of the month the power both in the arm and the leg had greatly increased: he could turn his wife's mangle with the arm without pain or fatigue; he could stand steadily and strongly upon the leg, and stamp the foot on the ground with some vigour. On the other hand, during the ten weeks from the time of the fit to the time of the first puncture, *no* progress, of any note, had been made; whereas each puncture (save two) seemed to add fresh vigour to the muscles. More jerking of the muscles occurred after the last few than after the first punctures.

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April 24th, 1864.—This man again came under treatment, not for paralysis, but for *cramp* of the *same* leg. For six weeks he had hardly passed a night free from four or five attacks of cramp which *came only* in the leg that had been paralysed.

I gave him a quarter of a grain of morphine subcutaneously; no cramp in the night; a slight twinge in the morning.

26th.—Three attacks of cramp in the night. Repeated morphia injection.

May 24th.—No cramp since.

October, 1866.—Keeps well; able to turn the mangle, and carry parcels about, the leg remaining as strong as when the puncture was omitted.

Case 3.—James N—, a sailor, æt. 28. Came under my care on the 25th of May, 1866.

He had received a bullet fourteen months before in the dorsal region when at Shanghai. The bullet had entered close to the posterior border of the right scapula, and is somewhere deeply imbedded close to the spinal marrow. Paralysis came on gradually from that time; but it became much worse after he had been shipwrecked off Hong Kong eight months ago. He was two months in the hospital at the latter place. Strychnine was there given him by the mouth for some weeks; it caused jumping in the leg which is paralysed, but did not increase the power of the muscles.

He now walks very slowly and carefully with two sticks, and drags the left leg almost like a log; sensation is much impaired; leg still jumps occasionally, and would give way at once if he were to try his weight on it; has pain in the back and loins after walking many minutes.

It was doubtful to what extent power could be restored in this case if, as seemed probable, the bullet was mechanically interfering with the transmission of nerve power, the more especially as strychnine, as above mentioned, had already been given by the mouth *without effect*.

On May 25th, 1866, I injected the $\frac{1}{24}$th of a grain of strychnia into the cellular tissue of the upper arm, and on the 27th, the same amount into that of the leg.

28th.—Can put the foot more firmly on the ground. Some jumping of the leg after both punctures; no jumping of the right leg.

28th and 30th.—Repeated the same dose. Leg decidedly stronger and feels as if it now belonged to him, no longer like a heavy weight;

can lift the foot higher, and he can now (after five punctures) just momentarily bear his weight on the foot without pressing on his sticks.

June 9th.—I diminished the dose to the $\frac{1}{36}$th of a grain still injected every second, third, or fourth day.

29th.—Can now walk two hours without feeling fatigue, and without that pain in the leg and loins which used always to occur after very small efforts. The leg now feels quite supple and "sensible."

July 23rd.—Up to this date this man has had twenty-six injections from the 25th of May, just over two months, and altogether has had less than *one* grain injected during that time. The following are the chief results from the last few punctures. The $\frac{1}{36}$th of a grain suits him better than the $\frac{1}{24}$th of a grain; it causes much less jumping, at the same time it always causes the leg to feel lighter and looser, and as if life had come into the heavy useless painful weight it formerly was to him.

October 28th.—He comes up once a week from Barnes to report progress. He can now easily walk three miles without stopping to rest, and without pain in the loins, and can walk across the room without his sticks. These good effects still remained when I saw him nearly one year after I had ceased to attend him.

Case 4.—Several injections of strychnia were given to a young woman who for some years had suffered from incessant muscular jactitations, frequent attacks of sickness, pain, and debility of the spine. The doses injected were from the $\frac{1}{48}$th to the $\frac{1}{24}$th of a grain. This patient had received great benefit from the atropia injection, and was not told that the agent injected was different.

The chief effects observed by her were a sensation of warmth in the spine, of greater strength and less pain in the muscles of the neck; the sickness of stomach was also removed by it.

Case 5.—Mr. W—, a publican, came to me on the 23rd of March, 1866. For the last three weeks he had complained of numbness of the legs and feet, of the sensation of pins and needles in the latter, and a fear of walking without holding or looking to see his feet. Is a sallow, puffy, unhealthy-looking man, temperate, bowels regular, urine often loaded with lithates, and difficult to pass at times, no albumen in it. Has the tight pain or band across the stomach. I put this patient upon alkalies, and the $\frac{1}{24}$th of a grain of strychnia twice a day by the mouth. He improved a good deal, sold his business, and went into the country.

On October the 23rd, he came back to London. Had been going on pretty well until three weeks ago, when his legs again stumbled and he could now only walk slowly and with difficulty. Urine again loaded with lithates, more loss of power over bladder, bowels, &c. I ordered him alkaline saline by the mouth for the state of the kidneys, &c., and this time gave him the strychnia subcutaneously, with the following results:—Decided increase of power of muscles of the legs and hips; he could, after five punctures, get up from sitting on a low chair, without supporting himself as before with his hands. Usually feels a warmth of both legs, increased diaphoresis, "live-blood" as it were circulating in his thighs, generally also a stiffness, but no jerking thirty minutes after each puncture, less fear of falling when walking, diminution of the numbness and trembling of the legs, and increased walking power.

He had ten punctures altogether, some in the arm and some in the thigh. The doses were from $\frac{1}{48}$th to $\frac{1}{36}$th of a grain.

Case 6.—John B—, æt. 31. Came to me in March, 1866, with loss of power of the muscles of the left arm and forearm, consequent upon bruising and dislocation of the shoulder-joint some weeks before. Most of the bruise had disappeared, but the power did not return, as indeed it often will not for months; he could not grasp anything, nor pick up things. I ordered an iodine and camphor liniment for some days without benefit resulting, and then had recourse to the injection of strychnia.

This man had seven punctures; three of which were into the muscles themselves, and four into the cellular tissue of one arm or the other. The chief effects observed by this patient were, 1st. He felt the influence usually in ten to fifteen minutes, viz., tingling in the fingers of the affected limb, some pains in, and increased temporary power of the muscles of the arm.

The power returned quicker in the muscles of the arm than did the activity to the fingers.

He did not notice any difference in the time in which the effect was produced, whether the injection was made into one arm or the other; but thought the fingers felt its influence most when the strychnia was injected into the pronator muscles. The dose in this case varied from the $\frac{1}{48}$th to the $\frac{1}{24}$th of a grain.

Case 7. — William B—, left hemiplegia. Came to me November 30th, 1867. Has had left hemiplegia for two years and a quarter, since a fit, which came on suddenly after two or three previous threatenings in August, at Madras; he was a soldier at the time. The left leg now drags, and he cannot walk (with his stick) more than fifteen minutes without the leg becoming stiff and painful; constantly has cramp in it at night, usually three or four times. The arm is very useless, and the mouth is still partially drawn; he seems very nervous, and frequently laughs when he should not; sleeps well, bowels regular, tongue clean, frequent micturition, urine healthy.

January 30th.—Has had eighteen punctures in two months, with the following results:—Feels generally stronger, not only in the limb which is paralysed, but "in himself." Has much more control over his muscles. He looks less foolish, and hardly laughs now as before without occasion. Always feels "warmer all over" after each puncture; feels more power and warmth for some hours in the leg after the injections, which were all made into the cellular tissue of one of the arms.

In this man it is the arm, contrary to my experience in the majority of cases of hemiplegia, which has received the most benefit; he can grasp much firmer with it, and hold weights which he could not when he first came; he is less nervous, and looks as if he now had some energy and will of his own; it is also interesting that the cramps in his leg which used, for many months, to wake him up at night, have never returned the last six weeks. This patient is still under treatment.

Remarks. — The effects obtained from the hypodermic use of strychnia are not so remarkable as are those which are constantly to be observed from the injection of atropia or of morphia. This is easy of explanation. Anodynes and narcotics are agents acting especially on nerves of sensation, and on nerve-centres, and are most valuable thus employed in acute affections, such as delirium tremens, acute mania of intense pain, &c. Strychnia is a nerve-tonic, and nerve-excitant, and its employment is chiefly valuable in cases of palsy and nerve atony, after all acute symptoms or causes have subsided. But because the case is one in which time is required to assist the action of the remedy, there can be no reason against trying to shorten the period required for the cure, or to limit the amount of the drug from which we expect benefit to accrue.

The chief advantages to be derived from the hypodermic use of strychnia are,

1st. *As a therapeutic test,* for three or four injections will almost always show if strychnia has any power or not over that particular palsy. If they have no effect it is almost useless to continue their employment.

2nd. *It is economical, both as regards amount of* (*a*) *alkaloïd to be used, and* (*b*) *time required for it to affect the system.*

(*a*) There is a great saving of the *amount of strychnia* required by this means over the stomachic employment of the same drug. The saving may be put at five-sixths of the amount which would be given by the mouth. For, as far as my observation goes, the $\frac{1}{30}$th of a grain, injected every other day for thirty times, will consume just one grain of strychnia in sixty days: now if the somewhat ordinary dose of $\frac{1}{20}$th of a grain is given twice a day—and some physicians order the $\frac{1}{16}$th and even the $\frac{1}{12}$th of a grain for a dose as it is evident that, in the sixty days, as much as six grains of strychnia are taken into the stomach. But, in cases of paralysis, where its continuance seems necessary, I do not, as a rule, inject the strychnia more often than twice a week, so that the saving is nine rather than six times less than the amount which experience shows us has to be given by the mouth for a reasonable amount of benefit to ensue.

Nor need this saving of material be considered remarkable nor the results singular. The experience of many medical men who have largely employed quinine injections in ague and fevers in India, Italy and the West Indies, is quite in accordance with my results with strychnia. Dr. Moore, of the Bombay Medical Service, thinks four or five grains of quinine under the skin are equal to five or six times that amount taken by the mouth; and this opinion is confirmed by Drs. Chasseaud and McCraith of Smyrna, by Dr. Desvigne in France; and more recently by Dr. Huggins and his colleague at San Fernando in Trinidad.

(*b*) In addition to the ultimate tonic effects of the strychnia being more quickly gained, and from a smaller amount of material, we have also manifested, by its introduction into the cellular tissue, certain phenomena indicative of the immediate or direct primary action of the agent upon the system. These are, 1stly, a general warmth or glow of the cutaneous surface. This warmth is experienced by nearly every patient, especially those benefited by the injection.[1] It is most felt in the paralysed limbs and down the spine, and at times making the patient "quite hot all over." This sensation lasts a few hours, according to the strength of the dose. 2ndly, a sensation of lightness and freedom in, and a removal of the "heavy-weight" sensation of the paralysed part. The leg often feels "light as a cork," and, 3rdly, increased temporary power which also generally begins in about twenty minutes, and lasts for perhaps some hours.

As regards the jerking of the muscles. This symptom of the action of strychnia appears to me to be of less frequent occurrence than when strychnia is given with a similar object in view for a lengthened period by the stomach. It seems practically to be the case, as might theoretically be conceived, that the primary tonic effects—namely, greater power and improved nervous sensibility—should follow the small strychnine injections, sooner and more effectually, than after the system has, by slow degrees, absorbed enough strychnia which has been administered stomachically, and the quantity of which so given has been perhaps three or four times as much as has really been necessary. When, on the other hand, muscular "twitchings," spasms, or cramp, have accompanied the palsy or numbness previous to the employment of the strychnine injection, those irregular muscular movements seem very quickly to yield to the tonic influence of the puncture, as in case 7, and in a bricklayer now under treatment.

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[1] Diaphoresis is a more frequent effect from the injected strychnia, especially of the paralysed side of the body. The warm glow is always observed by patients to be entirely or *chiefly* in those parts supplied by the paralysed nerves, even when the strychnia is injected into remote healthy parts.

Thus far, then, in favour of the hypodermic injection of this alkaloïd. What, on the other hand, are the disadvantages of this method?

That great care is necessary lest too large a quantity should be injected of this agent, I need not point out: far better, therefore, always is it to inject a minimum than a maximum dose, say from the $\frac{1}{60}$th to the $\frac{1}{80}$th rather than from the $\frac{1}{30}$th to the $\frac{1}{20}$th. As a rule, however, the $\frac{1}{36}$th of a grain will suit most cases in which a tonic effect is desired upon a paralysed muscle or nerve.

I think it as well to mention that in two out of about twenty-five patients in whom I have injected strychnia a carbuncular state of the nose, or rather a collection of small boils arose. It is questionable to what extent, or whether or not, the strychnia injection is to be blamed. We know that belladonna will, at times, produce a rose-rash, and this is especially the case with atropia, its alkaloïd, when injected.

Both of the patients who had the boils produced about the nose, had had a good many injections; one was the sailor with the gunshot wound in the spine whose case is mentioned above; and the other was an Indian officer who had for years suffered from neuralgia and muscular prostration, consequent on—according to Brown-Séquard—" congestion of the spinal marrow."

I have seen no ill results from the injection of strychnia such as have been described as following the injection of the acetate or sulphate of quinine. Those salts seem, in many cases, to have set up severe irritation, and subsequent sloughing of the cellular tissue, and even tetanus has been attributed in two cases to the injection of that alkaloïd. Strychnia is, however, innocuous to the cellular tissue, and scarcely ever causes the least smarting, burning, or other local sign of irritation, when injected. Nor would quinine, as far as my experience goes, if some more basic salt than those above alluded to was used.

Note.—As the action of strychnia is chiefly manifested upon the *muscular system*, whether taken in large or small doses, whether producing muscular jerkings and spasms or simply increase of power or tone, it may be asked, whether the result would not be more efficacious still if the strychnia was injected into the muscular tissue itself rather than into the contiguous or superjacent cellular tissue?

My reply to this question, from having practically tried both methods, is—

1. That I do not find any real advantage or any material difference of action when the muscles themselves are injected.[1]

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[1] There is, moreover, the disadvantage attending the injection of the muscles

2. Nor do I find any difference of effect upon paralysed muscles whether the strychnia is injected into the paralysed side of the body or the healthy side.

I have in some cases performed the injection alternately upon the healthy and the paralysed limbs. The results have been the same. The glow, if felt most on the paralysed side when that side is injected, is still felt there most if the injection is made into the other side of the body. Nor when the paralysis is chiefly confined to a few muscles have I found the effect greater (except perhaps in case 6) from the localisation. That patient, however, found the injured deltoid as much acted on whether the injection was made *into that or the other* deltoid.

I know Behier and others hold greatly with the necessity for localisation, and the author of a review upon the hypodermic treatment in the 'Archives Générales' amuses himself when he says—

"Pushing still further the theory of M. Hunter, we ought to admit that the hypodermic method enjoys a special efficacy when the puncture is made distant and very far from the painful spot."[1]

This observation was drawn forth from the critic, who could not understand how some cases of sciatica had been so successfully treated by myself by the injection into the arm; and as he has pushed my theory for me so far, I must state that even that which he proposes in ridicule may sometimes be the best in its effect; and I believe that a puncture made at a *distance* from the painful nerve *may be more* efficacious if it is made into a part *more vascular,* more full of *absorbents* and *blood-vessels,* than may be the part in which the painful nerve is situated.

Indeed, I originally proposed the view which, much as it was at first opposed, is now becoming universally conceded, that—

Localisation is not Necessary.

Such is the reason why some of my cases of sciatica treated by the injection into the arm have so astonished those surgeons who still look on the subcutaneous injection as simply a *local mode of treating a painful spot* rather than, as I first maintained, *an important means of rapidly producing the pure effects of soluble drugs upon diseases, whether affecting the system locally only as neuralgia, or generally, as in tetanus, chorea, and paralysis.*

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that one is apt to have an escape of a drop or two of blood. It must also be recollected that the muscle is a compact tissue, and less readily receives the fluid injected than the cellular tissue does. To avoid an external escape of blood it is best to make the puncture into the muscle by a separate movement from that which passes the needle through the skin.

[1] 'Archives Générales,' Janvier, 1866, "Revue Critique de la Médication Hypodermique."

For the Library.

Notwithstanding the carping of a few, it is to [illegible] great satisfaction that my view of the non-necessity for localisation, which I have for years been endeavouring to establish, has been so thoroughly corroborated by the experiments of the committee appointed especially to investigate the method by the Royal Medical and Chirurgical Society, whose conclusions are almost word for word those which I laid before the profession in 1859.[1]

[1] Compare the conclusions of the Committee at page 28 of the 'Report on Hypodermic Injection,' 1867, with the conclusions of the author in the 'Medical Times and Gazette,' of October the 8th, 1859, and also pp. 54—56 of the 'Memoir on the Speedy Relief of Pain and other Nervous Affections by the Hypodermic Method,' 1865.

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